REMARKS/ARGUMENTS

Priority

The Examiner notes that a certified copy of Italian application MI2002A 001684 has yet to be filed in the present case. Applicants would like to inform the Examiner that a certified copy of said application is being mailed concurrently with the electronic filing of this Response.

In the Specification:

In the specification, paragraphs [0040], [0042] and [0045] have been amended only to correct typographical errors contained therein.

In the Claims:

Claims 19 and 34-41 remain pending in the present application. Claims 2-18 and 20-33 have been canceled in this Response. Claim 1 was canceled in a previously filed preliminary amendment.

Rejection of Claims 11-12, 26, and 30-34 Under 35 U.S.C. § 112

The Examiner rejected claims 11-12, 26 and 30-34 under 35 U.S.C. § 112, first paragraph, based on a previously filed amendment that added language limiting the amount of THAM used to "above 4.0 mg/ml to 30 mg/ml." Applicants have deleted claims 2-19 and 20-33, thereby obviating the Examiner's rejection of claims 11-12, 26, and 30-33. Applicants also note that the 5/31/05 amendment referred to by the Examiner did not impart the recited THAM limitations to claim 34. As such, the Examiner's § 112, first paragraph rejection of claim 34 should be withdrawn.

Rejection of Claims 2-41 Under 35 U.S.C. § 112

The Examiner rejected claims 2-41 under 35 U.S.C. § 112, first paragraph, as containing insufficiently described subject matter. Particularly, the Examiner argues that there is not a single species of the claimed genus disclosed that is with in the scope of the claimed genus, *i.e. any nasal peptide fragment*. Applicants have canceled claims 2-18 and 20-33. Applicants also respectfully disagree with the Examiner's assertions. For example, the Examiner's attention is directed to the description as filed, from page 8, line 6 to page 9, line 3, wherein a long list of desirable physiologically active nasal peptides are disclosed, including also their pharmaceutically acceptable salts and their peptidic fragments.

Rejection of Claims 2-41 Under 35 U.S.C. § 102(b)

The Examiner rejected claims 2-41 under 35 U.S.C. § 102(b) as being anticipated, or in the alternative, under 35 U.S.C. § 103(a) as being obvious over Veronesi et al. (EP 0726075A). Applicants have canceled claims 2-18 and 20-33. As Applicants do not believe Veronesi et al. to teach or suggest the subject matter of the remaining rejected claims, the rejection is respectfully traversed.

First, although THAM is known to be useful in various pharmaceutical formulations, including some nasal formulations, Applicants assert that the present invention represents the first time that this material has been recognized as having absorbefacient properties. This constitutes a new and totally surprising use of THAM. It is also worth noting that this new use has the highly advantageous practical effect of enhancing the nasal peptide bioavailability level. To that end, the attached report

provides specific experimental evidence of the significant absorbefacient properties of THAM.

Furthermore, the Veronesi et al. reference cited by the Examiner teaches pharmaceutical non-inorganic saline solutions for endo nasal administration containing a peptide (a calcitonin), meglumine or glucamine, citric acid, polyvinylpyrrolidone and tromethane (THAM). Veronesi et al. is directed to overcoming the problem of the remarkable instability of calcitonins – not to using THAM as an absorbefacient as described in the present application. It will be noted that throughout Veronesi et al., the presence of the tromethane (THAM) is described only with respect to providing a partial buffering agent for citric acid, in particular to maintain the pH at 4.6 to 6.0. Nowhere, however, is there any teaching or suggestion that tromethane (THAM) is capable of exhibiting enhanced absorbefacient properties. Thus, Veronesi et al. does not anticipate the method of the present invention as recited in the remaining rejected claims.

Nor does Veronesi et al. render obvious the remaining rejected claims. Rather, one skilled in the art would understand that the use of THAM as a buffer is a completely different and completely unrelated technical effect to the use of THAM for its absorbefacient effects. To suggest otherwise would imply that a person skilled in the art would naturally look in the field of buffering agents when looking for useful compounds that provide absorbefacient effects. This is simply not the case. Therefore, Applicants' discovery that THAM produces enhanced absorbefacient properties of a pharmaceutical formulation is totally surprising and absolutely not rendered obvious by Veronesi et al. Consequently, Applicants respectfully submit that Veronesi et al. cannot support a

rejection of the remaining rejected claims under 35 U.S.C. § 102(b) or, in the alternative, under 35 U.S.C. § 103(a).

Report on the Enhanced Absorbefacient Properties of THAM

The present invention concerns a method for imparting to a nasal composition the ability to reversibly depolarize the nasal mucosa epithelial cells, and selectively enhance the permeability and improve the efficiency of active absorption of a pharmacologically active nasal peptide or pharmacologically active salt thereof or pharmacologically active fragment thereof through the nasal mucosa epithelial cells, by using a therapeutically effective amount of said peptide or salt or fragment together with THAM [tris(hydroxymethyl)aminomethane], as a selective absorbefacient.

In order to assist the Examiner in recognizing the significant absorbefacient ability of THAM to enhance the absorption of pharmacologically active nasal peptides, Applicants have conducted *in vivo* experiments that are presented in the attached report. In the associated study, pharmaceutical nasal formulations containing a known peptide, either desmopressin or insulin, were prepared according to the Formulations 1 to 12 presented in Tables n. 1 and n. 4 described in the report. Each nasal formulation was administered to an individual and then a blood sample was taken after 45 minutes to determine the maximum level of the peptide at that time. Attention is drawn to nasal Formulation 3 in the attached report, which corresponds to Formulation A described in Example 1 of the present application. From the results presented in Tables n.3 and n.6 in the report, it is extremely clear that THAM produces a significant increase in the absorption of pharmacologically active nasal peptides.

By contrast, results from Formulations 0(1-6) desmopressin and 0(7-12) insulin, deprived of THAM showed a poor absorption performance, as reported also in the above Tables.

CONCLUSION

Applicants have canceled claims 2-18 and 20-33, and have addresses the Examiner's § 112 rejections as to the remaining claims. Applicants have also distinguished the subject matter of the present invention over the teachings of the reference cited as prior art by the Examiner.

Therefore, Applicant respectfully submits that the present application is now in condition for allowance, and such action is earnestly requested. Telephone inquiry to the undersigned in order to clarify or otherwise expedite prosecution of the present application is respectfully encouraged.

Respectfully submitted,

Date: 09/27/2007 By: /Eric M. Gayan/

Eric M. Gayan
Attorney for Applicant
Registration No. 46,103
Standley Law Group LLP
495 Metro Place South
Suite 210
Dublin, Ohio 43017-5319
Telephone: (614) 792-5555
Facsimile: (614) 792-5536
E-mail:egayan@standleyllp.com